

# AN UPDATE ON EXERCISE AND DIET IN PARKINSON'S DISEASE

Dr. Mary S. Feldman



# PARKINSON'S DISEASE

- **Dr. James Parkinson, 1817**
- **Diagnostic Criteria**
  - **Bradykinesia and at least 1 of the following:**
    - **Rigidity**
    - **4-6 Hz resting tremor**
    - **Postural instability**
  - **And Rule out “red flags”, mimickers, and Parkinson’s plus syndromes**

# NEARLY 1.5 MILLION PEOPLE HAVE PARKINSON'S DISEASE IN THE USA

- Progressive neurodegenerative condition, 2<sup>nd</sup> only to Alzheimer's disease in incidence
- 60,000 new cases diagnosed in the US each year
- Annual treatment costs approaching \$25 billion

**ETIOLOGY**  
*MULTIFACTORIAL*

**Complex interplay between**

**Genetics**

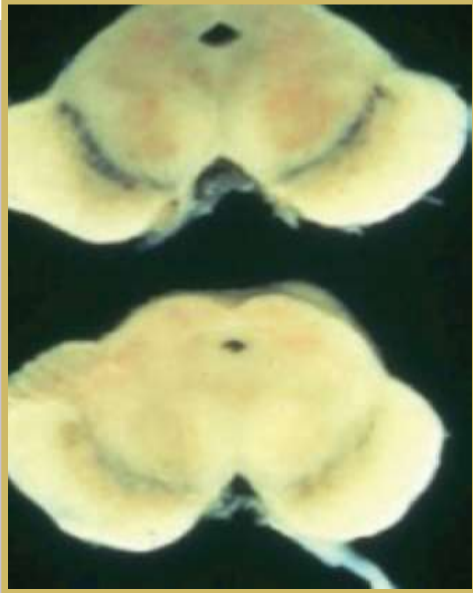
**Environment**

# PATHOPHYSIOLOGY - *MULTIFACTORIAL*

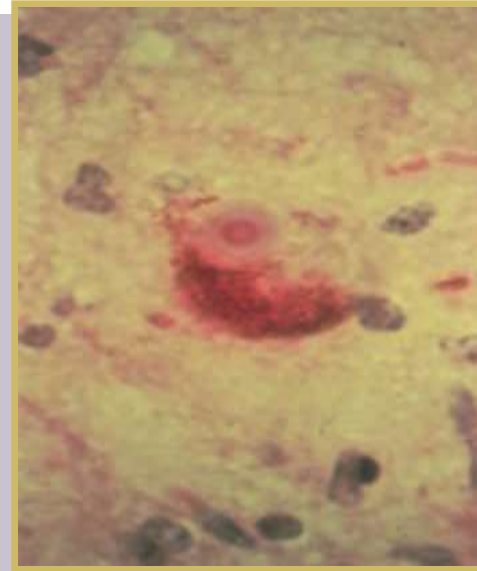
- **Mitochondrial dysfunction**
- **Oxidative Stress**
- **Neuro-inflammation**
- **Excitotoxicity**
- **Abnormal deposition of proteins (lewy body)**
- **Dopamine neuronal cell loss in the substantia nigra**

Ferretta et al. *Biochimica et Biophysica Acta*. 1842 (2014). 902-915

# NEURONAL DEGENERATION AND PROTEIN DEPOSITION



**Significant nigral  
dopaminergic neuronal loss  
is marked by a reduction in  
neuromelanin pigment in  
the SNpc**



**The lewy body:  
intraneuronal  
cytoplasmic inclusion  
with proteaceous halo**

Images from Olanow CW, Stern MB, Sethi K. The scientific and clinical basis for the treatment of Parkinson disease (2009). *Neurology*. 2009;72(21 suppl 4): S1-S136. Farrer MJ. *Nat Review Genetics*. 2006;7:306-318.

# NEURONAL DEGENERATION AND PROTEIN DEPOSITION

**By the typical time of DIAGNOSIS – a patient typically  
has lost about 50-80% of the substantia nigra  
dopamine neurons**

# TREATMENT OPTIONS...

- MAO-B inhibitors
- Amantadine
- Dopamine Agonists
- Levodopa
- Anti-cholinergics
- COMT-inhibitors
- Deep Brain Stimulation/Lesioning
- Complementary and Alternative Medicine and Therapies (CAM)
  - Surveys find as many as 76% of PD patients use CAM



# TREATMENTS...

**The single most important unmet medical need in Parkinson's disease is a **neuroprotective** therapy...**

- **Olanow, 2008.**
- **Steady PD III trial – Isradapine, 2015**
- **Adagio trial, 2011 - ? Rasagaline. FDA – says NO on neuroprotection, but very controversial.**

# EXERCISE AND PARKINSON'S DISEASE

- **Attractive Adjunct... Empowers the patient**
- **Little (if any) “side effects”**
- **Improves mood**
- **Strengthen muscles/tone**
- **Supports Brain Plasticity**

# **EXERCISE ABSOLUTELY PREVENTS PARKINSON'S DISEASE!! (NO DOUBT)**

## **Several Major Prospective Studies Done:**

- 1) Neurology, 2005. Chen et al. Followed 48,575 men. 252 developed Parkinson's disease. Vigorous exercise was associated with a 60% reduction in the development of Parkinson's**
- 2) Neurology, 2010, Xu et al. Physical Activity and Future Risk of Parkinson's disease. Followed 213,701 patients over 10 years. 767 patients developed PD. Moderate to Vigorous activity patients was associated with a 40% lower risk of Parkinson's disease**
- 3) Brain, 2015. Swedish National Cohort. 48k men and women. Moderate levels of overall physical activity were associated with 60% Parkinson's risk reduction.**

# EXERCISE AND NEUROPLASTICITY

- Research has shown that exercise (aerobic) increases neurotrophic proteins, including brain-derived neurotrophic factor (BDNF), and glial derived neurotrophic factor (GDNF), and others within the basal ganglia and striatum which protects against cell loss.
- There is a molecular and cellular response to acute exercise in the release of neurotrophins – which are key in supporting neuroplasticity.

Knaepen et al. Neuroplasticity – exercise-induced response of peripheral brain-derived neurotrophic factor: a systematic review of experimental studies in human subjects. *Sports Med.* 2010. 40(9). 765-801.

# WHAT KIND OF EXERCISE IS BEST...?

- The Jury is out.
- Any kind THAT you will STICK WITH!!
- Research studies show mixed results. Why?

Variability of exercise  
type used  
patients used  
small sample sizes  
difficult to have a control group  
“dose” of exercise  
mode  
intensity

# RESEARCH ON SPECIFIC EXERCISE TYPES...

## Tai Chi

- There have been 7 RCT's published in the past decade on the PD population.
- Studies consistently demonstrate Tai Chi groups have consistently better scores on measures of postural stability, recorded fewer falls, had better motor outcomes, and had better quality of life scores (QOL) than control groups (no exercise).
- Safe, feasible. Class I evidence by AAN guidelines.

# RESEARCH ON SPECIFIC EXERCISE TYPES...

## Dance

- 6 published RCT's of Tango dancing in PD within the last decade – one group comparing to conventional exercise and only the Tango group showing improved balance scores, all others compared to “no exercise”.
- **Motor, balance, and gait scores improved in all patients who were exercising regardless of what exercise they were performing.**
- Good quality studies; Class I or II AAN evidence

Duncan et al, 2014. The Journal of Alternative and Complementary Medicine; Bega, et al. Curr Treat Options Neurol, 2014. 16: 314.

# RESEARCH ON SPECIFIC EXERCISE TYPES...

## Yoga

- One small RCT – 13 patients over 12 weeks comparing yoga to “no exercise” control group.
- No comparisons were made for Yoga vs other exercise.
- Patients doing yoga vs no exercise had better **UPDRS motor scores and balance scores.**

Colgrove et al. 2012; Effect of Yoga of on motor function in people with Parkinson's disease: a randomized controlled pilot study. J yoga Phys Ther. 2012; 2(112).



# RESEARCH ON SPECIFIC EXERCISE TYPES...

## Aerobic Exercise

Studies consistently show improvements in fitness, fatigue, depression, QOL, motor scores, and show neuroprotective effects in animal models.

It appears that generally, the higher the effort – the more brain derived neurotrophic factors are released – and possibly more “neuroprotection”.

# AEROBIC EXERCISE...

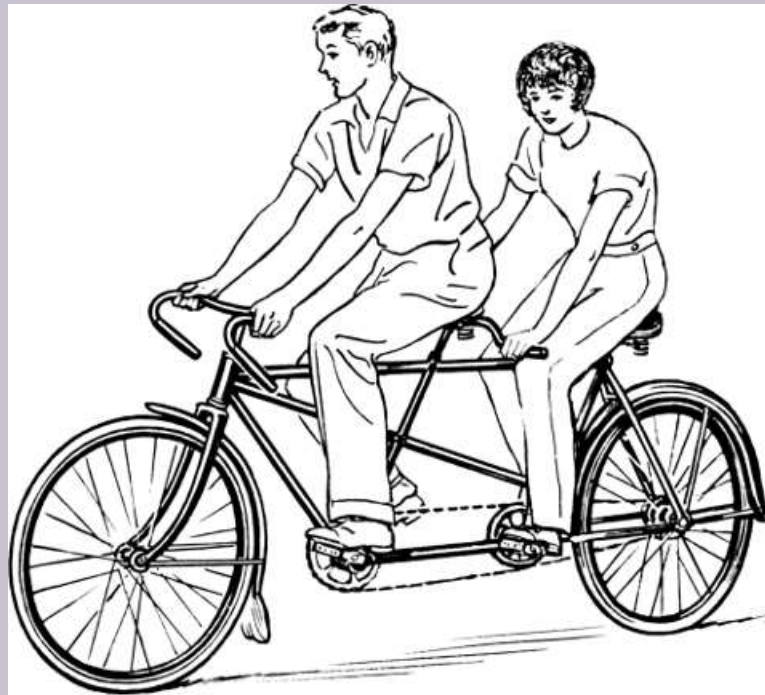
- **Appears to be the best type of exercise for releasing the most neurotrophins (aside from forced exercise).**
- **Stay within your target heart rate for your age**
- **Check with your doctor first to see if it's safe for you to engage in an aerobic exercise program from a cardiovascular standpoint.**

# “FORCED EXERCISE”

- Model of aerobic exercise in which a Parkinson's patients rate of exercise is augmented mechanically to assist them in achieving and maintaining an exercise rate that is greater than their preferred voluntary rate of exercise.
- Higher exercise rate, i.e., forced exercise (FE) has demonstrated to release more neurotrophic factors, has proven to be more dopamine sparing, and has shown improved motor functioning.

Alberts et al. Forced, Not Voluntary, Exercise Improves Motor Function in Parkinson's Disease Patients. *Neurorehabil Neural Repair*. 2009. 600-608.

# TANDEM BIKE FOR “FORCED EXERCISE”



# “FORCED EXERCISE”

Alberts et al. performed a RTC using a group of PD performing voluntary exercise vs FE on a tandem bike model.

Patients exercised 3 times a week for 8 weeks for 1 hour.

- FE groups maintained a cadence of about 86 rpm's; avg heart rates were around 117 BPM
- Voluntary maintained a cadence of about 60 rpm's; avg heart rates were around 121 BPM

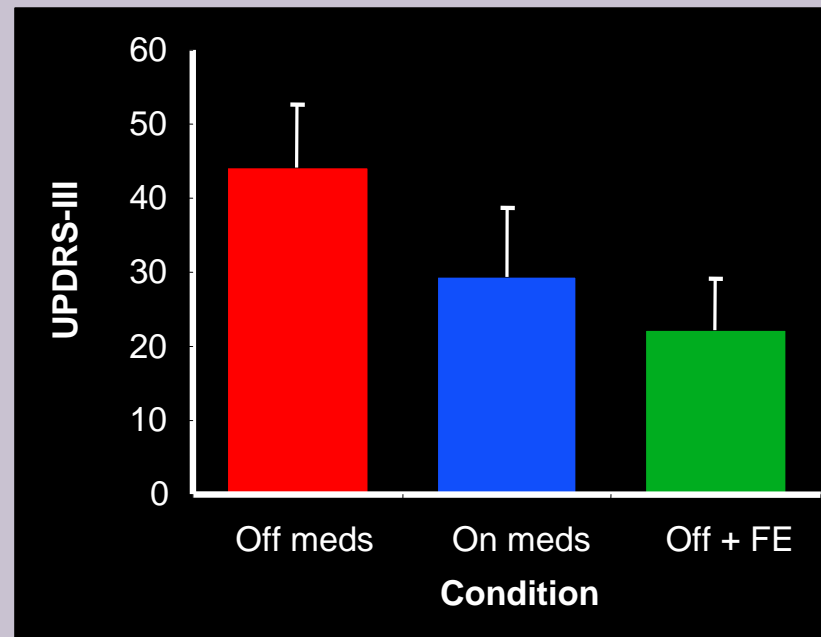
# “FORCED EXERCISE”

- Patients evaluated “off” meds, UPDRS III
- In the FE group:
  - 41% improvement in rigidity,
  - 38% improvement in tremor, and
  - 28% improvement in bradykinesia
- (Voluntary groups improved, but only about half as much).

# “FORCED EXERCISE”

- **Functional MRI scanning was done 3 hours after a 40 minute session of forced exercise, as well as “on” and “off” meds.**
- **The pattern of cortical and subcortical activation was similar while patients were on medication and 3 hours post FE – indicating that medications and FE utilize similar pathways to produce symptomatic relief.**

# FORCED EXERCISE – BETTER THAN “ON”



Alberts et al. Forced, Not Voluntary, Exercise Improves Motor Function in Parkinson's Disease Patients. *Neurorehabil Neural Repair*. 2009. 600-608.



# “THERACYCLE”

\$5,499.00 (can buy on sale for around \$3000).



# NUTRITION IN PARKINSON'S DISEASE

***“Let Food be your medicine and medicine be your food”***

- - Hippocrates, 400 A.C.

- *“Man is what he eats”*

- - Ludwid Andreas Feuerbach, 1864



# INHERENT PATHOPHYSIOLOGY...

- **Mitochondrial dysfunction**
- **Oxidative Stress**
- **Neuro-inflammation**
- **Excitotoxicity**

# NUTRITION IN PARKINSON'S DISEASE

## *Can be tricky*

- **Protein interactions with levodopa**
- **Constipation**
- **Weight loss over time**
  - **Dyskinesia**
  - **Loss of smell/taste**
  - **Nausea due to medications**
  - **Feel full secondary to dysautonomia**

# LOWER PARKINSON'S RISK....

- **With High Caffeine/Coffee intake**
- **Strong Protective Effect also seen with Black Tea Consumption (NOT green tea)**
- **Cigarette Smokers (although BAD for you in many ways!!)**
- **PD risk appears to be lower in light/moderate alcohol use compared to NON-alcohol use and heavy drinkers (multiple studies)**

# NATURAL COMPOUNDS...

## NEUROPROTECTIVE??

- Creatine – doesn't help, Class I evidence, RTC 1500 pts.
- Co-enzyme Q 10 – QE3 trial was not shown beneficial compared to placebo
- Vitamin E – DATATOP study, 1993, no help compared to placebo.
- Curcumin (tumeric) - known to reduce inflammation, being investigated.
- Glutathione (IV) – no convincing benefit in studies of neuroprotection.
- Acetyl- L-carnitine – may prevent mitochondrial dysfunction and oxidative damage in cellular models. Being investigated.

# VITAMIN D

- Beneficial to monitor and normalize
- Levels are naturally lower in Patients with Parkinson's disease... why...?
- Recent study (Shen and Ji, *Nutrients*, 2015), found an association between vitamin D status, and risk of Parkinson's disease by studying 5690 patients. Patients with lower levels or deficiency of Vit D more likely to develop Parkinson's disease.
- Associated with more depression, physical symptoms, cognitive impairment.

# "DIETS" IN PARKINSON'S DISEASE

## *Mediterranean Diet*

- Higher adherence to a Mediterranean diet associated with lower risk of Parkinson's disease, Alcalay et al. Movement Disorders, 2012.
  - 257 PD patients vs 198 controls
- Foods: vegetables, legumes, fruits, cereals, fish, regular and moderate consumption of alcohol – particularly in the form of wine with meals... (lower consumption of meats/animal fats)



# “FRENCH PARADOX”

- Population in the south of France, despite eating a diet relatively high in saturated fats, presents a low risk of heart disease.
- Resveratrol – neuroprotective polyphenol in the Mediterranean diet?

Lopez- Miranda et al. Resveratrol: a neuroprotective polyphenol in the Mediterranean diet. *Rev Neurol*. 2012. 54(6); 349-56.

# RESVERATROL

- Ferretta et al. 2013 tested Resveratrol on patients with a genetic Parkinson's disease (Parkin mutation).
- They found that Resveratrol caused a significant increase in mitochondrial ATP content and an overall increased metabolic capacity.
- Resveratrol alleviates mitochondrial dysfunction in fibroblasts by coordinating signaling pathways in which AMPK is involved.

# RESVERATROL

*Basically –*

**DRINK RED WINE!!!!**



# OLEOCANTHAL – VIRGIN OLIVE OIL

- **Reduces incidence of chronic inflammatory disease**
- **Shares unique anti-inflammatory properties characteristic of ibuprofen**
- **Studies done that demonstrate that it plays a role in reducing neuro-inflammation, reduces Tau formation, and helps clear amyloid-Beta. (beneficial in Alzheimer's disease – and therefore most likely helps in PSP – Progressive Supranuclear Palsy Pathology).**

# KETOGENIC DIET FOR PARKINSON'S DISEASE?

- No proof that this helps Parkinson's disease.
- Investigated for neuroprotective properties
- Used successfully in Epilepsy

# CHOLESTEROL LEVELS....

- Higher Total Levels of Cholesterol, especially monounsaturated, leads to LOWER risks of Parkinson's disease.
- Statins do NOT offer a neuroprotective benefit. (use of statins caused higher risk of Parkinson's disease).

# “VELVET BEAN” FOR PARKINSON’S

- **Mucuna Puriens – contains naturally occurring dopamine. Used by some as an “alternative treatment” option for L-dopa.**
- **Not modulated by the FDA as it’s considered a “supplement”.**
- **A recent study published in the Journal of Scientific Reports in 2015 reported that they studied various species of Mucuna Puriens and found that the M. pruriens degraded into ROS (reactive oxygen species and damaging quinones which is neurotoxic to the brain).**

# **“BEST DIET” FOR PARKINSON’S DISEASE**

- **One high in fiber (to prevent constipation)**
- **High in water/hydration (to help support blood pressure, and also to help with constipation)**
- **High in fruits/veggies (because of antioxidant properties)**
- **Green leafy veggies**
- **Legumes/beans**
- **Fish**
- **Olive Oils**
- **Lean Meats in limited quantity**
- **Limited red meat/limited fried foods**
- **1 glass of red wine with meals is ok**
- **Healthy whole grains**
- **(AND PLENTY OF EXERCISE!!!!!!)**

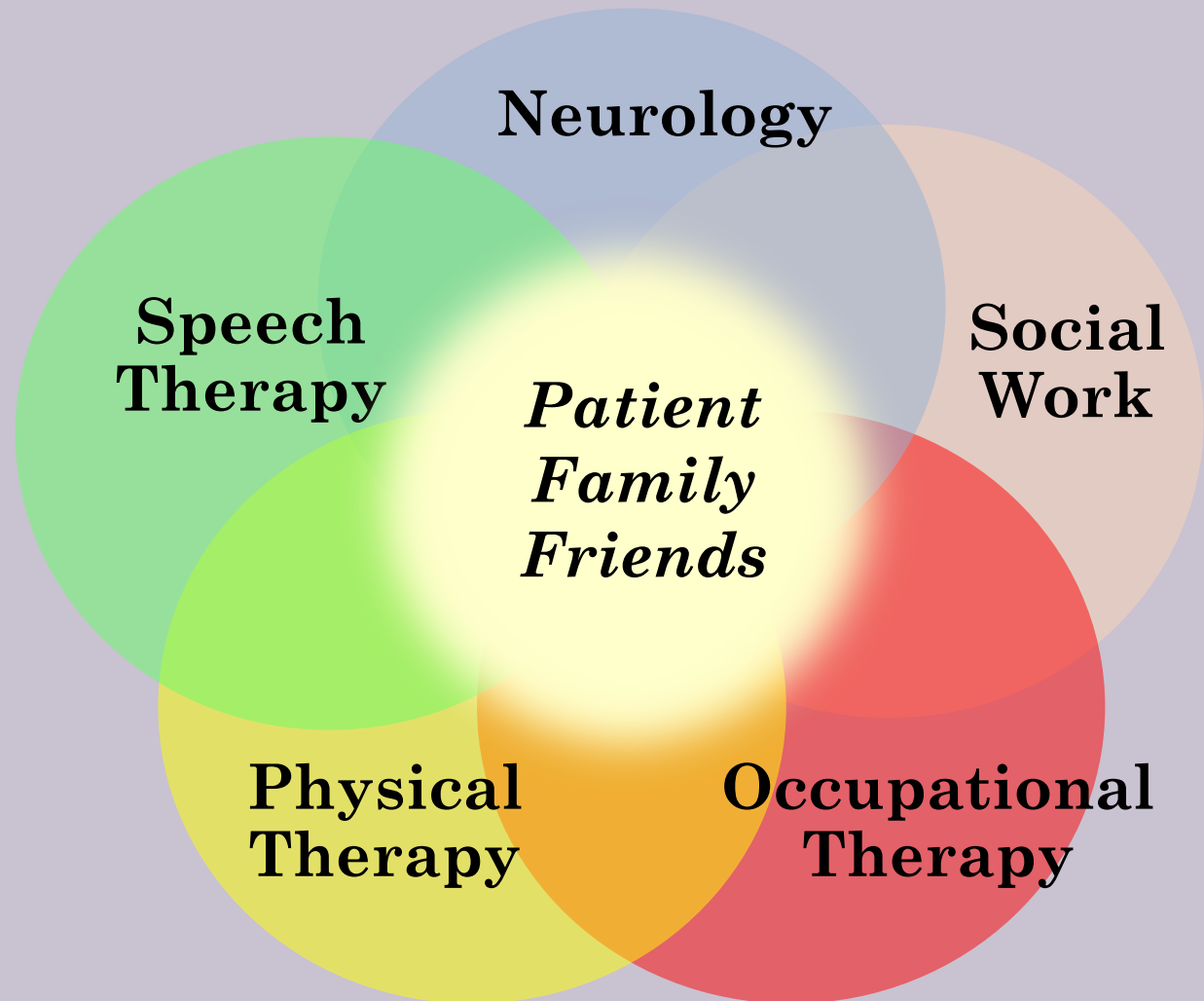


# OUR FUTURE VISION AT DHMC...



# INTERDISCIPLINARY PARKINSON'S CENTER AT DARTMOUTH HITCHCOCK

**Primary  
Care  
& Other  
Providers**



**We need Your Help and Support to  
Make this a Reality !!**

**Thank you!!**